

# CELLECTIS

ANNUAL REPORT 2017





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# Note from the Chairman and CEO —



Last year we took several important steps towards our goal of using gene-editing therapies to save lives. Thanks to encouraging preliminary clinical results, we now have clear confirmation that allogeneic gene-edited CAR-T product candidates are a new paradigm in oncology. UCARTs are here to stay.

As the pioneer in gene editing, Cellectis is firmly on course to deliver safe and effective next-generation CAR T-cells, using our high-precision, flagship TALEN® technology, to address unmet medical needs in oncology. The benchmarking shows clearly that these product candidates are very potent. There are now two UCARTs in clinical phase, UCART19 and UCART123, a rich pipeline with proven targets, and potential quick wins over the next three years with several Investigational New Drug filings in the U.S.



Here are some highlights from 2017:

**UCART19**, which we exclusively licensed to Servier, is an allogeneic CAR T-cell product candidate, developed to treat adult and pediatric patients with relapsed or refractory (R/R) acute lymphoblastic leukemia (ALL). Currently in Phase I, UCART19 has the potential to overcome the limitations of the current autologous approach.

At the 59<sup>th</sup> American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta in December 2017, our partner Servier presented preliminary results from two Phase I studies of UCART19 carried out with its partner, Pfizer. These first-in-human data showed an 83% complete remission rate across the adult and pediatric patients population.

- > In the **CALM (UCART19 Advanced Lymphoid Malignancies)** study, a Phase I, open label, dose-escalation study designed to evaluate the safety, tolerability and anti-leukemic activity of UCART19 in adult patients with R/R B-ALL, five out of seven patients treated achieved molecular remission at Day 28 post-UCART19. Molecular remission is defined by negative minimal residual disease (MRD). MRD is a measurement of the number of residual leukemic cells that remain after treatment.
- > In the **PALL (Pediatric Acute Lymphoblastic Leukemia)** study, a Phase I, open label study designed to evaluate the safety and ability of UCART19 on pediatric patients, results showed all five children achieved MRD negativity, enabling them to proceed to allogeneic stem cell transplant. Only one Grade 1 cutaneous acute GvHD occurred. No severe neurotoxicity was observed. Cytokine release syndromes were mild in the majority of cases, and all were manageable.



**These first-in-human data demonstrated the safety and tolerability of UCART19, resulting in an 83% complete remission rate across the adult and pediatric patient population.**

**UCART123**, our first wholly-controlled product candidate, is a gene-edited T-cell investigational drug that targets CD123, an antigen expressed at the surface of leukemic cells in acute myeloid leukemia (AML), as well as on leukemic and other tumoral cells in blastic plasmacytoid dendritic cell neoplasm (BPDCN). In February 2017, it became the first allogeneic, “off-the-shelf” gene-edited CAR T-cell product candidate to receive FDA approval for Phase I clinical trials in patients with AML and BPDCN.

The clinical trials began in June 2017 with a first patient suffering from AML treated at Weill Cornell Medicine and New York-Presbyterian. This was followed by a first patient enrollment for BPDCN in August at the MD Anderson Cancer Center. This patient died from a premature death post UCART123 injection leading to a clinical hold by the FDA.

The study resumed in November 2017 with protocol changes. AML is a devastating clonal hematopoietic stem cell neoplasm with an estimated 21,000 new cases per year in the U.S. alone. BPDCN is a disease of bone marrow and blood cells but also often affects skin and lymph nodes. We will expand these trials to other centers to include more patients in 2018.

Development plans for our other product candidates are proceeding steady. Following preclinical proof of concept in 2016, **UCART22**, which targets acute lymphoblastic leukemia and other B-cell malignancies, has proven to be highly efficient at eradicating tumors *in vivo*. After conducting preclinical studies in collaboration with MD Anderson Cancer Center, in May 2018 we submitted an IND to the FDA requesting approval to initiate a Phase 1 clinical trial for UCART22 in acute lymphoblastic leukemia (B-ALL). Pending regulatory clearance, Cellectis plans to initiate a Phase 1 clinical studies in the second half of 2018. The clinical research will be led by Dr. Nitin Jain, Assistant Professor, and Prof. Hagop Kantarjian, Chairman in the Department of Leukemia and University Chair in Cancer Medicine at The University of Texas MD Anderson Cancer Center in Houston.

Acute lymphoblastic leukemia (ALL) is a rapidly progressing form of leukemia that is characterized by the presence of a large number of immature white blood cells in the blood and bone marrow. In 2016, an estimated 6,590 new cases were diagnosed in the U.S., with over 1,400 deaths due to ALL. Approximately 85 percent of ALL cases involve precursor B-cells (B-ALL).



**UCARTCSI** targets multiple myeloma, a large unmet medical need with 30,000 patients a year in the U.S. and a high relapse rate. UCARTCSI has shown durable *in vivo* efficacy, with ongoing preclinical studies at MD Anderson Cancer Center. Manufacturing this year for clinical trial use is ongoing and we plan on an IND filing in 2019.

In 2017, we became strongly confident that TALEN® is the best suited gene-editing technology for developing next-generation cancer therapies. TALEN® enjoys strong intellectual property, precision targeting, and a consistent 95% knockout efficiency, making it the most powerful gene-editing technology in biotechnology as of today.

**Our technology also has the potential to deliver healthier food ingredients to benefit consumers.**

In 2017, we also strengthened our team with two senior appointments:

- > Prof. Stéphane Depil, MD, PhD, to the role of Senior Vice President Research & Development and Chief Medical Officer. Prof. Depil's responsibilities include bringing Cellectis' product candidates to clinical-stage development, strategic and operational management of all therapeutic activities, and supervising research and development projects for the Company. He remains adjunct Professor at Léon Bérard Cancer Center and University Claude Bernard Lyon 1, France.
- > Elsy Boglioli to the role of Chief Operating Officer. Ms. Boglioli's responsibilities include

directing the long-term strategy and current business priorities of Collectis to ensure that the overall mission of the Company is fulfilled. Ms. Boglioli joined Collectis from Boston Consulting Group (BCG), where she was Partner and Managing Director and leader of BCG's biotech-focused business in Europe.

The applications of the TALEN® gene-editing platform go well beyond medicine. Our technology also has the potential to deliver healthier food ingredients to benefit consumers. Following its Initial Public Offering on Nasdaq in July 2017 resulting in gross proceeds of \$64 million, **Calyxt**, our plant sciences subsidiary (NASDAQ: CLXT), is firmly on track for the commercial launch this year of the first gene-edited product in the world ever to be commercialized: a healthier oil that has no trans fats and reduced saturated fats.

As Chairman of Calyxt, in which Collectis retains a nearly 70% ownership stake as of May 31<sup>st</sup>, 2018, I am proud of the Company's achievements in leveraging gene editing to develop healthier food products. With a strong management team and new, cornerstone shareholders, last year Calyxt joined the Farmer Business Network seed distribution program, expanded its product portfolio, and worked to complete a new facility on 10 acres in Roseville, Minnesota, scheduled to open in 2018.

Gene editing presents great promise for the future of medicine, but it also raises some questions about where we are headed. As pioneers in this field, we take these questions seriously and hope to engage many others - including scientists, medical doctors, politicians, lawyers, religious leaders and philosophers - in a general discussion.

**The big advantage of Collectis is our tremendous experience in the gene editing field.**

We believe Collectis is the leader of the gene-editing space, thanks to its deep expertise in this field. We have a strong understanding of DNA recombination processes as well as a strong and seasoned team of long time gene-editing experts.

We also have a rich, diversified intellectual property portfolio comprised of 175 patent families, 163 granted patents, and 737 patent applications (as of January 1, 2018) along with solid strategic partnerships with Servier and now with Allogene who share our willingness to developing allogeneic cancer therapies that will benefit patients around the world.

With a strong and fully committed team, solid financial resources, and a clear mission, Collectis is well positioned for powerful growth. First of all I wish to thank our shareholders for their strong and continuous support. I would also like to warmly thank the Collectis and Calyxt teams for their dedication, support, and belief in our mission. In 2018, we will continue to work on the new immuno-oncology product candidates and food products that will revolutionize both agriculture and medical care, making the world a safer, healthier place for everyone.



# Who we are Collectis —



## 101

employees at Collectis

81 in Paris, France

20 in New York, NY



## 13

**wholly-controlled product candidates**  
targeting hematological malignancies,  
solid tumors and other indications



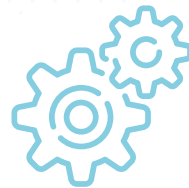
## 3

product candidates in clinical  
trials targeting ALL, AML,  
BPDCN, B-ALL



## 26

scientists dedicated to  
research and clinical  
development



## 39

people dedicated to  
the manufacturing process  
and analytics



## 2

**clinical supplies manufacturing  
sites in Europe:** CELLforCURE  
(France) & MolMed (Italy)



# Calyxt



43

employees at Calyxt  
all in Minnesota



24

scientists dedicated to  
Research & Development



7

products declared non-regulated articles under the "Am I Regulated?" process by **Biotechnology** Regulatory Services of the Animal and Plant Health Inspection Service (APHIS), an agency of the United States Department of Agriculture (USDA)



19

Products under development across 5 crops: soybean, wheat, alfalfa, canola and potatoe

– Who we are

# Mission Statement

Collectis is a clinical-stage biopharmaceutical company developing a new generation of cancer immunotherapies based on gene-edited T-cells (UCART). Capitalizing on 18 years of expertise in gene editing – built on its flagship TALEN® technology and pioneering electroporation system PulseAgile – Collectis uses the power of the immune system to target and eradicate cancer cells. Derived from healthy donors rather than the patients themselves, allogeneic CAR T-cells will make it possible to develop cost-effective, off-the-shelf products that are capable of being cryopreserved, stored and distributed worldwide.

CAR-T-based immunotherapy is one of the most promising areas of cancer research, representing a new paradigm for cancer treatment. UCART is the first therapeutic product line that we are developing with our gene-editing platform to address unmet medical needs in oncology.

This concept has now been validated by ongoing clinical studies investigating UCART19, UCART123, UCART22 and UCARTCS1 product candidates, which show their potential as powerful tools in fighting cancer.

In addition to our focus on immuno-oncology, we are exploring the use of our gene-editing technologies in other therapeutic applications, as well as to develop healthier food products for a growing population. Calyxt, our subsidiary based in Minnesota, aims to create healthier food products such as high oleic soybean oil,

**Derived from healthy donors rather than the patients themselves, allogeneic CAR T-cells will make it possible to develop cost-effective, off-the-shelf products that are capable of being cryopreserved, stored and distributed worldwide.**

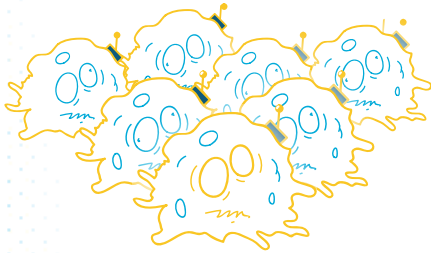
high-fiber wheat, cold storable potatoes, and low saturated canola oil to benefit consumers.

Collectis is listed on the Nasdaq market (CLLS) and on Euronext Growth (ticker: ALCLS). Following an IPO in July 2017, Calyxt is listed on the Nasdaq market (CLXT).



— Who we are

# 2017 Highlights —



## APPOINTMENTS

**Nine Prominent Physicians to Join Collectis Clinical Advisory Board**

January 23, 2017; March 07, 2017

**Appointment of Hervé Hoppenot and Rainer Boehm, M.D. to Board of Directors**

June 28, 2017

**Appointment of Elsy Boglioli to Executive Vice President, Strategy and Corporate Development; Chief Operating Officer**

December 04, 2017

**Appointment of Immuno-Oncology Leader Stéphane Depil as Senior Vice President Research & Development and Chief Medical Officer**

December 04, 2017

## THERAPEUTIC ADVANCES WITH UCART123

**IND Application for UCART123, an Allogeneic Gene-Edited CAR T-Cell Product Candidate, in AML and BPDCN**

January 03, 2017

**IND Approval to Proceed with the Clinical Development of UCART123, the First Gene-Edited Off-the-Shelf CAR T-Cell Product Candidate developed in the U.S.**

February 06, 2017

**First-in-Human Administration of UCART123 in Collectis' AML Phase 1 Clinical Trial at Weill Cornell Medicine, New York-Presbyterian Hospital**

June 27, 2017

**Collectis' UCART123 Administered to First Patient with BPDCN in Phase 1 Clinical Trial at MD Anderson Cancer Center**

August 17, 2017

**Clinical Hold on Collectis Phase 1 Clinical Trials with UCART123 in AML and BPDCN Lifted after 2 months**

November 06, 2017

## THERAPEUTIC ADVANCES WITH UCART19 (LICENSED TO SERVIER)

Servier and Pfizer announced FDA clearance of IND application for UCART19 in Adult Relapsed/Refractory Acute Lymphoblastic Leukemia

March 09, 2017

Servier and Pfizer Announced Preliminary Results of the First-in-Human Trials of UCART19 Will Be Presented at the 59th American Society of Hematology (ASH) Annual Meeting

November 01, 2017

Preliminary Data from Servier and Pfizer's UCART19 Product Candidate Showed High Complete Remission Rate Across Two Phase 1 Adult and Pediatric Acute Lymphoblastic Leukemia Trials

December 12, 2017

## PATENTS AND PUBLICATIONS

Publication Studies Safety of Collectis' New CAR Architecture Controlling CAR T-Cell Functions

Published on January 23, 2017

Collectis Patent Encompassing Broad Uses of Gene Editing Technologies Maintained by USPTO

May 10, 2017

Collectis Granted Patent for CRISPR Use in T-Cells

July 24, 2017

Collectis Demonstrated Fine and Predictable Tuning of TALEN® Gene Editing Targeting to Improve T-cell Adoptive Immunotherapy

November 20, 2017



— Who we are

# Our core asset: Gene editing —

Gene editing is the ultimate application of genetic engineering in which DNA can be inserted, deleted, repaired or replaced from a precise location in the genome. Gene editing has many potential therapeutic applications. For example, it could be used to correct diseases and disorders that have a genetic basis. Just as editing text involves adding, removing, or replacing words, genome editing is an approach in which the physical composition of DNA is directly changed by adding, replacing, or removing DNA bases. Gene editing is going to change the way people are treated, potentially allowing to cure the roots of diseases instead of merely treating the symptoms. It provides us with the ability to rethink how we treat diseases altogether. It is the next transformative step in medicine.

**Gene editing is going to change the way people are treated by curing the roots of diseases instead of merely treating the symptoms.**

Collectis' proprietary nuclease-based gene-editing technologies, combined with our strong experience in gene editing, allow us to edit any gene with high precision. Our TALE nucleases, including a particular class of proteins derived from transcription activator-like effectors, act like DNA scissors to edit genes at precise target sites. Our approach is to edit immune cells to make them focus specifically on cancer cells by targeting an antigen and eradicating the cancer cells. One key component of this approach is T-cells, a type of white blood cell that plays an important role in identifying and killing foreign and malignant cells.

Three years ago, the first patients were treated by gene-edited CAR-T-cells to cure severe cases of leukemia. CAR-Ts are T-cells from the human immune system that are genetically modified with a gene coding for a Chimeric Antigen Receptor, or CAR. The CAR redirects the killing properties of these T-cells against a patient's cancer cells.

Gene-edited CAR T-cells are already used in the clinic today for some cancer therapies. Therapeutic gene editing will provide new ways of treating patients by correcting the genetic roots of their diseases, opening the door to the treatment of patients who are born with severe genetic disorders. It will also be useful in antiviral applications.





What we  
believe in —

– What we believe in

# Our vision —



At Collectis, we believe gene editing will completely reshape molecular medicine within the next decade. Our flagship TALEN® technology, combined with 18 years of experience in the gene-editing field, allows us to edit any gene with precise insertion, deletion, repair and replacement of DNA sequences in a living cell. Cells can now be engineered with optimized features for cancer therapies, genetic disease, viral therapy, drug discovery, industrial biotechnology, and more.

Our vision is to continue to leverage the potential of gene editing to deliver revolutionary products that address unmet medical needs. Our initial focus is to apply gene-editing to develop and commercialize best-in-class allogeneic CAR T-cell therapies in the area of immuno-oncology.

**The hope is that our “off-the-shelf” product candidates will transform the way we think about cancer care and serve as the next step in curing this disease through the power of gene editing.**

With this innovative approach, the hope is that our “off-the-shelf” product candidates will transform the way we think about cancer care and serve as the next step in curing hard to treat diseases.

At the heart of Collectis are the **allogeneic CAR T-cells** that can be sourced from healthy donors instead of the patients themselves. This “off-the-shelf” approach leads to lower production costs and enables us to deliver the product to the patient’s bed.

T-cells from one healthy donor, and one manufacturing batch of UCART create hundreds of doses of product and potentially more when scaling up the process. By removing the need



for personalized manufacturing of autologous therapies, off-the-shelf technology would make CAR-T therapy significantly cheaper than autologous CAR-T, thus removing a huge burden on healthcare systems. This would definitively offer a treatment option for many cancer patients across the world for whom scarce hope was left.

Gene editing will remain one of the main drivers not only in healthcare but also in agriculture. Through **Calyxt**, our plant subsidiary located near Minneapolis, our technology has the potential to deliver healthier food products for improved consumer health. By combining its leading gene-editing technology and technical expertise with its innovative commercial strategy, Calyxt is preparing to deliver healthier food for consumers and to the food industries. The objective is to deliver natural healthy ingredients that would benefit consumers.

Collectis was the first company in the world to develop gene editing, in 1999. We know how to modify any gene in an extremely safe and precise manner. We are a gene editing company at our core. Thanks to our business model, strong partnerships, and encouraging preliminary clinical results, we enjoy a significant lead entering this market. The 21<sup>st</sup> century will be the century of gene editing, and Collectis will be leading this revolution.

– What we believe in

## Universal cancer immunotherapies available to patients in need

Our leading immuno-oncology product candidates, which we refer to as UCARTs, are all allogeneic CAR T-cells engineered to be used for treating the largest number of patients with a particular cancer type. UCARTs are “off-the-shelf” therapeutic products, which means they are derived from pre-existing donor cells and not from the patient. As a result, production of UCARTs can be industrialized and thereby standardized over time and from batch to batch with consistent pharmaceutical release criteria. Each UCART product candidate targets a selected tumor antigen and bears specific engineered attributes, such as compatibility with specific medical regimens that cancer patients may undergo. Indeed, UCARTs represent a specific and powerful approach to treating any cancer patient with a given molecular

“signature.” UCART is our first therapeutic product line that we are developing with our gene-editing platform to address unmet medical needs in oncology.

Our approach aims to deliver an “off-the-shelf” product with the following benefits:

- > Broad availability. Enable products to be shipped globally, thereby reducing deployment obstacles and providing accessibility to a broad patient population;
- > Cost-effectiveness. Streamlined manufacturing process has the potential to reduce costs compared to autologous therapies;
- > Novel features. Develop products with specific safety and control properties;
- > Compatibility. Develop products taking into consideration the current standards of cancer care;
- > Consistency. Qualify and develop immunology products that are designed for optimal dosage, while reducing batch-to-batch variability.



Program	Indication	Product development	Preclinical	Manufacturing	IND Filing <sup>(1)</sup>	Phase I	Phase II	Phase III
UCART19 <sup>(2)</sup> (Servier/ Allogene)	ALL (PALL)							
	ALL (CALM)							
UCART23	AML							
	BPDCN							
UCART22	B-ALL							
UCARTCS1	MULTIPLE MYELOMA							

(1) Or European equivalent

(2) UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.

– What we believe in

# Gene-edited CAR T-cells: how it works

## From T-Cells to UCART products: the defense squad

The immune system protects the body from any foreign matters that might cause it harm. The success of the immune system depends on its ability to discriminate between foreign (non-self) and host (self) cells. Cancer cells thrive, in part, because the immune system treats them as self, even though they sometimes express abnormal antigens, and thus immune tolerance could occur when the immune system fails to recognize and attack tumors. Breaking immune tolerance is an important aspect of most immuno-oncology based therapies because it enables the immune system to recognize and treat tumors and leads to the eradication of tumor cells. We are using our gene-editing platform to develop gene-edited T-cells that express a Chimeric Antigen Receptor (CAR) and are designed to target and destroy cancer cells. CARs are artificial proteins that, when present at the surface of T-cells, enable the them to recognize a desired protein, or antigen, at the surface of the cancer cell and trigger the killing of cells harboring this antigen at their surface (target cells). Upon cell-to-cell contact between T-cells and cancer cells, antigen recognition will activate the effectors, giving them the signal to attack their targets, and leading to the killing of cancer cells.

## CARs (Chimeric Antigen Receptors)

CARs are engineered proteins that, when present at the surface of T-cells, enable them to recognize specific proteins or antigens that are present on the surface of a target cell and induce the killing of the target cell. CARs are today one of the most promising approaches to fight cancer through the development of immunotherapies. Indeed, immune cells (most often T-lymphocytes) are engineered to express a CAR able to recognize proteins present at the surface of cancer cells. CARs are constructed by assembling domains from different proteins, each of which enables the chimeric molecule to carry out specific functions. The most common CAR architecture comprises an extracellular domain containing **a region that recognizes the targeted antigen and a spacer region that links it to the transmembrane domain** (the part of the protein that spans the cellular membrane). This is followed by **an intracellular domain, responsible for transmitting an activation signal to the cell upon antigen recognition, causing the CAR-engineered cell to attack the tumor cell**. The target-binding moiety is usually derived from an antibody, while the intracellular portion can include, besides the domain leading to cell activation and cytotoxic response, one or more domains from **co-stimulatory receptor proteins that could enhance the proliferative capacity and survival of the “therapeutic” cells**. Cellectis is currently developing a collection of CARs targeting antigens present on cells from various types of cancer, as well as a proprietary multi-chain architecture of these artificial receptors, aiming to further increase the efficacy of adoptive cell therapies.

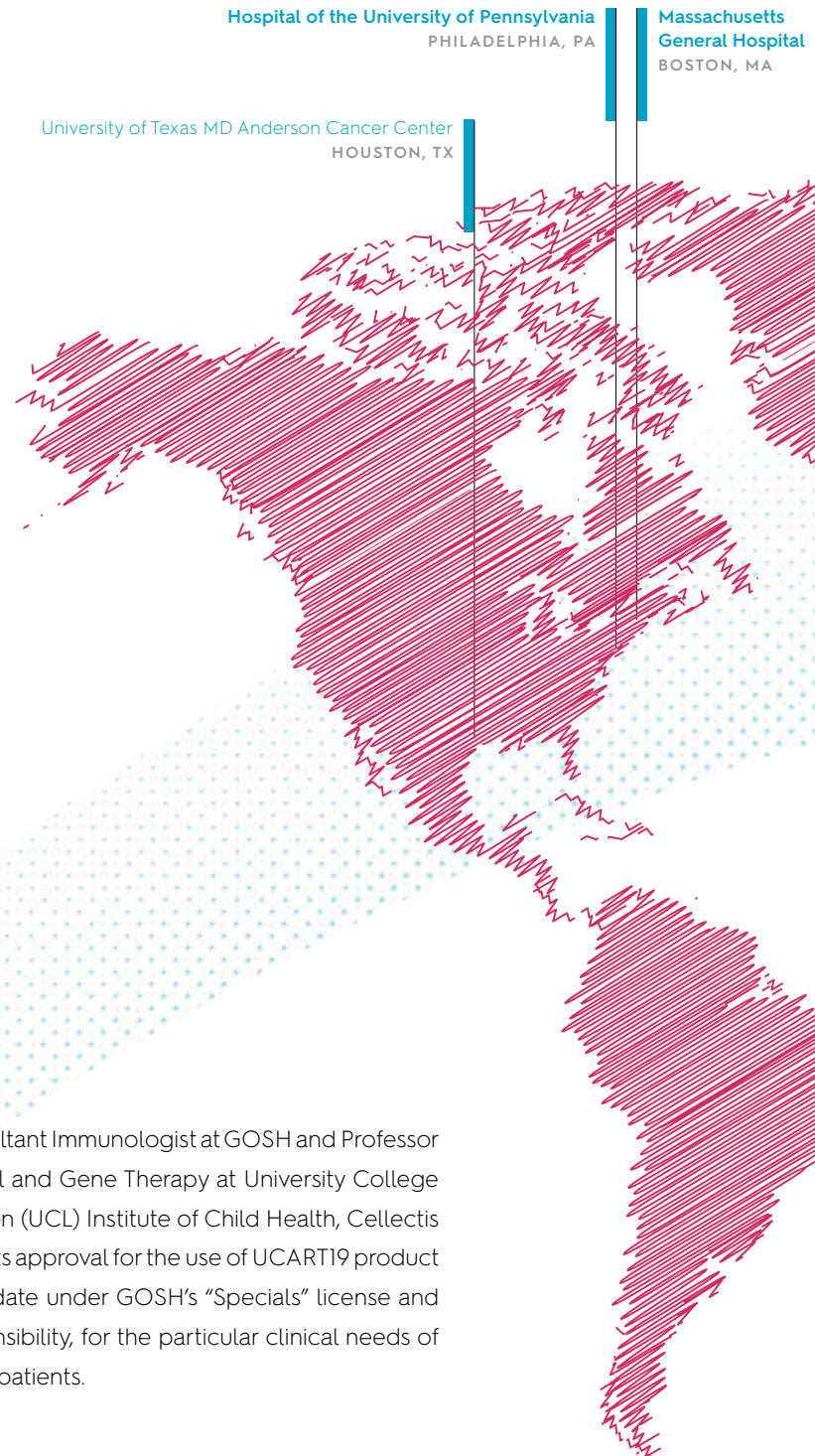
— What we believe in

# UCART19

UCART19, which we exclusively licensed to Servier, is an allogeneic CAR T-cell product candidate developed for treatment of CD19 expressing hematological malignancies, gene-edited with TALEN®. UCART19 is initially being developed in acute lymphoblastic leukemia (ALL). The initial approach with UCART19 is based on the preliminary positive results from clinical trials using autologous products based on the CAR technology, and has the potential to overcome some limitations of the current autologous approach by providing an allogeneic, frozen, “off-the-shelf” T-cell based product.

In a medical first, two young patients were treated with gene-edited off-the-shelf T-cells back in 2015. Each of the two infants had leukemia and had undergone previous treatments that failed, according to a description of their cases published in January 2017 in *Science Translational Medicine*. This first-in-human use of our TALEN® engineered UCART product candidate represents a landmark in the use of gene-editing technologies to save human lives. In 2015, Great Ormond Street Hospital (GOSH) treated these young patients under a special license from the Medicines & Healthcare products Regulatory Agency (MHRA) with the UCART19 product candidate because no other therapies were available for refractory relapsed acute lymphoblastic leukemia (ALL) following mismatched allogeneic stem cell transplantation. In response to an unsolicited request from Professor Waseem Qasim,

Consultant Immunologist at GOSH and Professor of Cell and Gene Therapy at University College London (UCL) Institute of Child Health, Collectis gave its approval for the use of UCART19 product candidate under GOSH’s “Specials” license and responsibility, for the particular clinical needs of these patients.



King's College Hospital NHS Foundation Trust  
UCL Great Ormond Hospital  
LONDON, UK

Het Kinderziekenhuis Prinses Elisabeth - UZG  
GENT, BELGIUM

### Clinical centers for UCART19 studies

CALM STUDY   
PALL STUDY 

The Christie NHS  
Foundation Trust  
MANCHESTER, UK

Hôpital Saint-Antoine  
Hôpital Saint-Louis  
Hôpital Robert-Debré  
PARIS, FRANCE

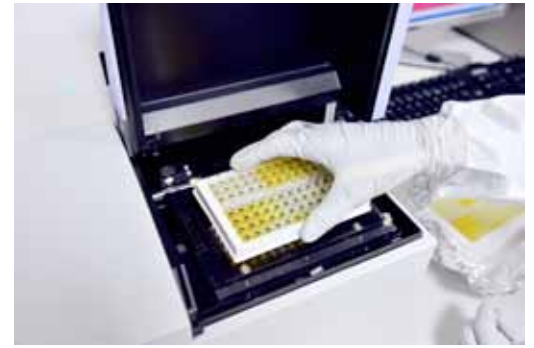


In November 2015, Servier acquired the exclusive rights to UCART19 from Collectis. Following further agreements, Servier and Pfizer began collaborating on a joint clinical development program for this cancer immunotherapy. In April 2018, Allogene Therapeutics, Inc. and Pfizer entered into an asset contribution agreement for Allogene to receive Pfizer's allogeneic CAR-T portfolio. As a result of the agreement, Allogene received certain exclusive rights to UCART19 in the United States, while Servier retains exclusive rights for the rest of the world.

In December 2017, Servier, Pfizer, and Collectis presented at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta preliminary results from two Phase 1 studies of UCART19: the CALM study at King's College London and MD Anderson Cancer Center, and the PALL study at Great Ormond Street Hospital. These first-in-human data showed an 83% complete remission rate across the adult and pediatric patient population. Servier is the sponsor of both studies that are active in Europe and the U.S.

The CALM study (UCART19 in Advanced Lymphoid Malignancies) is an open label, dose-escalation study designed to evaluate the safety, tolerability and anti-leukemic activity of UCART19 in adult patients with R/R B-ALL. The study was initiated in the U.K. in August 2016.

Five out of seven patients treated in the CALM study achieved molecular remission at Day 28 post-UCART19. Molecular remission is defined by negative minimal residual disease (MRD). MRD is a measurement of the number of residual leukemic cells that remain after treatment. Only one Grade 1 cutaneous acute graft versus host disease (GvHD) occurred. No severe



neurotoxicity was observed. Cytokine release syndromes (CRS) were mild and manageable except in one patient treated with UCART19 at the first dose level, who developed CRS Grade 4 and neutropenic sepsis leading to death at Day 15.

**First-in-human data demonstrated the safety and tolerability of UCART19, resulting in an 83% complete remission rate across the adult and pediatric patient population.**

The PALL study (Pediatric Acute Lymphoblastic Leukemia) is a Phase 1, open label study designed to evaluate the safety and ability of UCART19 to induce molecular remission defined by MRD negativity at Day 28 to enable allogeneic stem cell transplantation in pediatric patients with high-risk R/R B-ALL. PALL was initiated in the U.K. in June 2016.

Results for the PALL study showed all five children achieved MRD negativity, enabling them to proceed to allogeneic stem cell transplant. Only one Grade 1 cutaneous acute GvHD occurred. No severe neurotoxicity was observed. Cytokine release syndromes were mild in the majority of cases and were all manageable.

– What we believe in

# UCART123

Our first wholly-controlled product candidate, UCART123, is a gene-edited T-cell investigational drug that targets CD123, an antigen expressed at the surface of leukemic cells in AML, as well as on leukemic and other tumoral cells in BPDCN. Cellectis received in February 2017 an Investigational New Drug (IND) approval from the U.S. Food and Drug Administration (FDA) to conduct two Phase I clinical trials with UCART123 in patients with acute myeloid leukemia (AML) and blastic plasmacytoid dendritic cell neoplasm (BPDCN). This marks the first IND for an allogeneic, “off-the-shelf” gene-edited CAR T-cell product candidate granted by the FDA.

AML is a devastating clonal hematopoietic stem cell neoplasm that is characterized by uncontrolled proliferation and accumulation of leukemic blasts in bone marrow, peripheral blood and, occasionally, in other tissues. These cells disrupt normal hematopoiesis and rapidly cause bone marrow failure and death. In the U.S. alone, there are an estimated 21,000 new AML cases every year, with 10,000 estimated deaths every year.

The clinical research at Weill Cornell is led by principal investigator Dr. Gail J. Roboz, Professor of Medicine at Weill Cornell Medicine and Director of the Clinical and Translational Leukemia Programs at Weill Cornell Medicine and New York-Presbyterian.

BPDCN is a very rare and aggressive hematological malignancy that is derived from plasmacytoid dendritic cell precursors. BPDCN is a disease of bone marrow and blood cells but also often affects skin and lymph nodes.

The UCART123 clinical program at MD Anderson is led by Dr Naveen Pemmaraju, MD, Associate Professor, Dr Marina Konopleva, Professor, and Professor Hagop Kantarjian, MD, Department Chair, Department of Leukemia, Division of Cancer Medicine. On September 4<sup>th</sup>, 2017, the FDA put UCART123 clinical trials on hold following a death in the BPDCN studies.

On November 6, 2017, the FDA lifted the two-month clinical hold on both Phase I trials of UCART123 product candidate in AML and BPDCN. Patient enrollment has resumed since then.



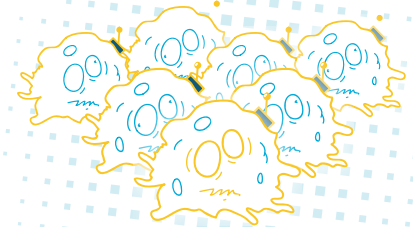
– What we believe in

# UCART22



UCART22 is an allogeneic, “off-the-shelf,” gene-edited T-cell product candidate designed for the treatment of B-ALL. Like CD19, CD22 is a cell surface antigen expressed from the pre-B-cell stage of development through mature B-cells and CD22 expression occurs in more than 90 percent of patients with B-ALL. In May 2018, Cellectis announced the submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) requesting approval to initiate a Phase 1 clinical trial for UCART22, Cellectis’ second wholly controlled TALEN® gene-edited product candidate, for the treatment of B-cell acute lymphoblastic leukemia (B-ALL) in adult patients.

Cellectis plans to initiate a Phase 1 clinical trial in the second half of 2018. The clinical research will be led by Dr. Nitin Jain, Assistant Professor, and Prof. Hagop Kantarjian, Chairman in the Department of Leukemia and University Chair in Cancer Medicine at The University of Texas MD Anderson Cancer Center in Houston.



– What we believe in

# UCARTCS1

UCARTCS1 is an allogeneic gene-edited T-cell product candidate designed for the treatment of CS1-expressing hematologic malignancies. UCARTCS1 is being developed in multiple myeloma (MM). Manufacturing of UCARTCS1 according to GMP is ongoing for purposes of conducting a clinical trial.



# Deep dive into manufacturing

GMP, or Good Manufacturing Practices, are a set of regulations applicable to the manufacturing of health product candidates, especially medicines intended for human use, such as UCART product candidates. In order to receive a license to manufacture pharmaceutical product candidates from governmental regulatory agencies, a company is required to comply with GMP regulations. The manufacturing department takes manufacturing processes established at the R&D level, converts them to GMP, and ensures their deployment with GMP compliant raw materials and environments. The department is responsible for the manufacturing of clinical trial material ("CTM"), making it available for clinical studies and afterwards, and also for the manufacturing of final GMP commercial cellular gene therapy products.

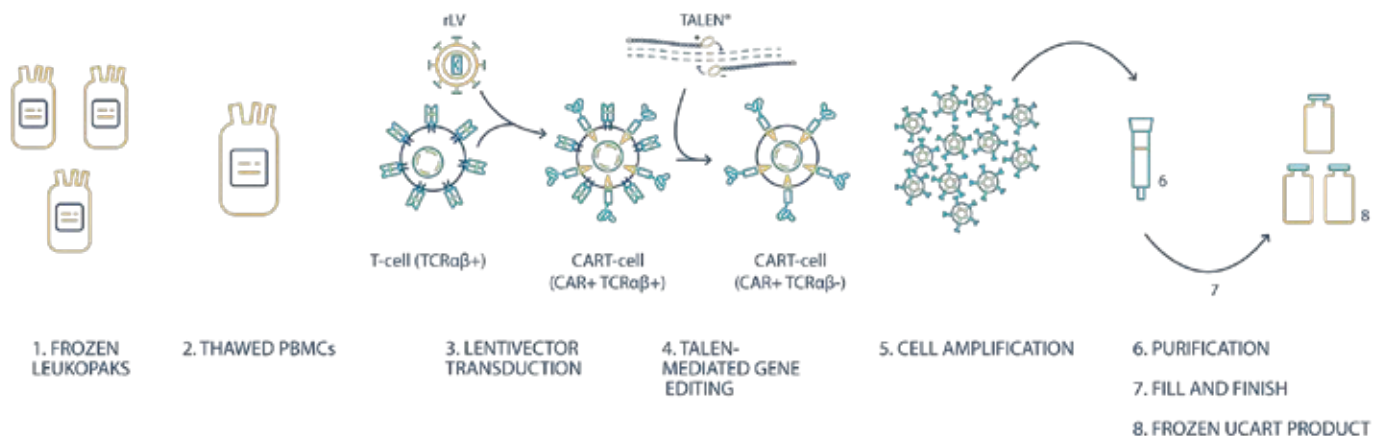
## Our proprietary manufacturing process

Through our manufacturing process, therapeutic UCART product candidates are made from healthy, tested and qualified donor T-cells; unlike

**One manufacturing batch of UCART, could be used to create hundreds of doses of product and more when scaling up the process.**

autologous CAR-T approaches all derived from patient samples. This "off-the-shelf" approach leads to lower production costs and will accelerate the administration of the treatment to patients. In addition, our process – powered by TALEN® and our proprietary PulseAgile electroporation technologies – inactivates genes in a highly efficient manner that avoids harming T-cells during processing. As a result, we can manufacture quality UCART with high yields – and potentially in bulk. We expect that T-cells from one healthy donor, and one manufacturing run of UCART, could be used to create hundreds of doses of product and more when scaling up the process. The objective of the manufacturing department is to increase yield and quality while reducing costs.

Collectis is working with two contract manufacturing organizations, CELLforCURE (France) and MolMed (Italy) to produce clinical batches of the UCART product candidates.

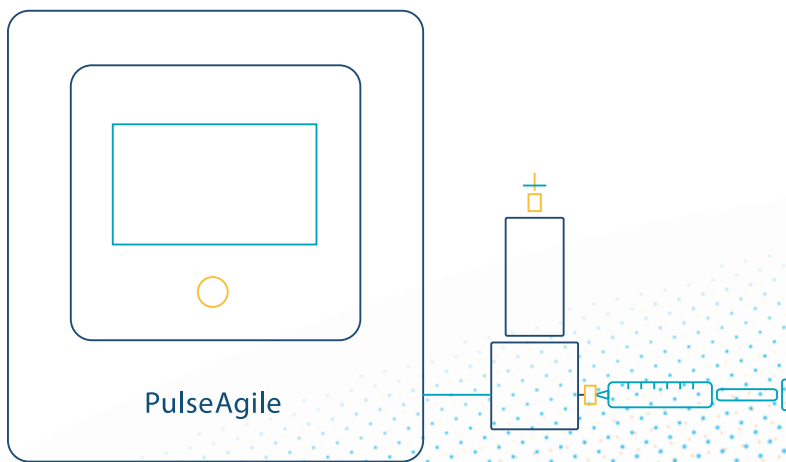


### PulseAgile: an indispensable technology to perform gene editing

PulseAgile electroporation technology uses a unique electrical field wave-form (see graph) that, in combination with a proprietary buffer solution, enables molecules, such as nucleases, to enter efficiently into the cell while maintaining high cell viability. PulseAgile uses a particularly effective combination of high voltage peaks, which are optimized to create transient holes in the cell membrane, followed by lower voltage pulses that help mRNA migrate into the cells. Critically, PulseAgile is optimized to preserve high cell viability and thus suited for large-scale manufacturing.

Importantly, PulseAgile provides a large volume platform for delivering nucleases-encoding mRNA into T-cells on an industrial scale, where it can be translated to generate an active nuclease protein that can access and specifically cut the cell's genomic DNA. The mRNA molecules are rapidly degraded by the cell, which means that the nucleases are only expressed for a short time during which they operate the intended precise surgical DNA modifications. PulseAgile is a key component of Cellectis high yields and high quality manufacturing.

PulseAgile provides a high-quality platform for delivering nucleases-encoding mRNA into T-cells



#### PulseAgile

Full optimized wave forms and frequency for better payload and viability.



Compared to:

#### Exponential decay

Limited in efficacy and cell viability.



#### Rectangular wave

Second generation wave. Repeat wave increase payload.



A person wearing a white lab coat and white gloves is shown in a laboratory setting. They are holding a large, clear plastic bag filled with a bright red liquid. The person is using a pipette to transfer liquid from a small vial into the bag. The background is a plain, light-colored surface.

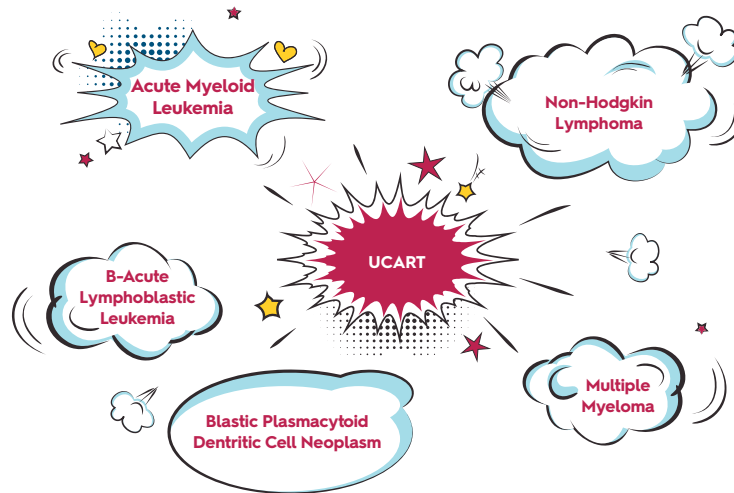
How our  
innovation could  
transform lives —

As Cellectis has always been at the forefront of innovation and technological advancements, implementing disruptive features in our products to meet unmet medical needs is a core aspect of our mission. In 2017, Cellectis invested \$79.2 million in Research and Development activities, which represents 62% of our total operating expenses. Cellectis is a pioneering gene-editing company at its core, focusing its know-how on elaborating immunotherapies using its expertise and its TALEN® gene-editing platform to develop off-the-shelf gene-edited T-cells that express

– How our innovation could transform lives

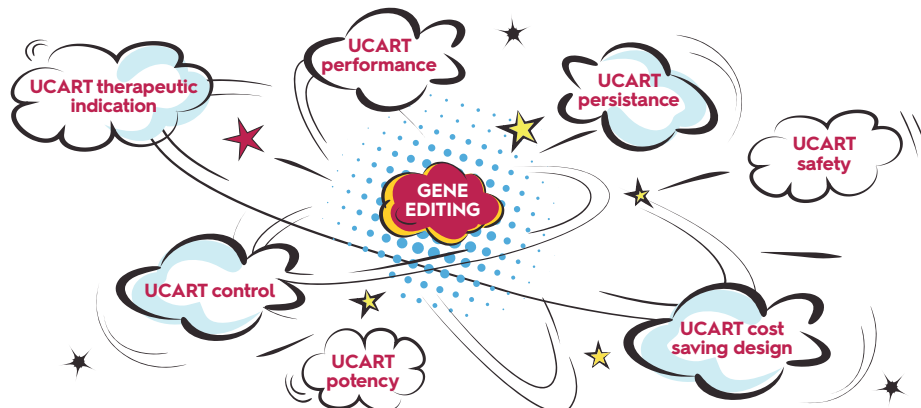
## Research & Development

Chimeric Antigen Receptors (CARs) to target and destroy cancer cells. The success of CAR T-cell based therapies relies on the capacity to identify and target antigens expressed on tumor cells. Cellectis is currently developing a pipeline of CARs targeting antigens present on cells from various types of cancer.



Using gene-editing technology, we are able to precisely and efficiently insert, replace, correct and/or inactivate genes at will. Cellectis is working on improving and expanding the potential of its allogeneic off-the-shelf UCART product candidates through gene editing by adding innovative features that will ultimately benefit patient treatments. Our goal is to improve engineered

CAR T-cells' functionalities through the molecular engineering of the CAR architecture (proprietary multi-chain architecture and proprietary CAR integrated suicide switch for safety), but also through multiplex gene editing thanks to our capacity to rapidly design optimal TALEN® combinations.



This expertise with the TALEN® molecular scissors associated with a synthetic biology type of approach allows us to rewire key T-cell functions to address CAR-based immunotherapy

challenges such as tumor environment, safety, or CAR-T's therapeutic indications, with the benefit of the patients always at the core of our ambition.

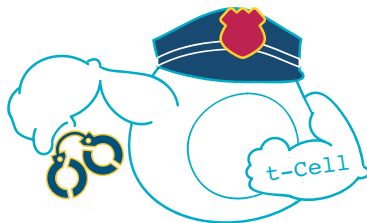
# Together we can do more





## Servier

In February 2014, we entered into a strategic collaboration agreement with Servier to develop and commercialize certain UCART candidates. In addition to the upfront payment, the strategic alliance, as amended in November 2015, has the potential to provide for aggregate additional payments of up to €887 million (\$966 million), comprising payments upon the exercise of each option granted to Servier and payments upon the occurrence of certain specified development and commercial milestones. We are also eligible to receive tiered royalties ranging in the high single-digit percentages based on annual net sales of commercialized products. This agreement covers the development and the



potential commercialization of the lead product candidate, UCART19, as well as other undisclosed product candidates directed at different targets. Under the terms of the agreement, we are responsible for the research and development of certain product candidates through the end of their respective Phase 1 clinical trials. We granted Servier an option to obtain an exclusive, worldwide license on a product candidate-by-product candidate basis, with respect to each target selected by Servier and developed under the agreement, to further develop, manufacture

and commercialize such products in the field of antitumor adoptive immunotherapy. Upon exercising each option, Servier will assume responsibility for the further clinical development, manufacturing and commercialization of the relevant product candidate.

In November 2015, we entered into an amendment to our initial collaboration agreement with Servier, which allowed for an early exercise of Servier's option with respect to UCART19 and other product candidates. Pursuant to this amendment, Servier exercised its option to acquire the exclusive worldwide rights to further develop and commercialize UCART19. In addition, Pfizer and Servier announced that they entered into an exclusive global license and collaboration agreement, under which Pfizer obtained exclusive rights to develop and commercialize UCART19 in the U.S. In April 2018, Allogene Therapeutics, Inc. and Pfizer entered into a definitive asset contribution agreement for Allogene to receive Pfizer's allogeneic CAR-T portfolio. As a result of the agreement, Allogene has received exclusive rights to UCART19 in the United States, while Servier retains exclusive rights for all other countries.

In 2017, UCART19 clinical trials are ongoing at UCL Great Ormond Hospital, London, UK, Hôpital Robert-Debré, Paris, France, and Het Kinderziekenhuis Prinses Elisabeth - UZG, Gent, Belgium, for the PALL study. For the CALM study, clinical trials are ongoing at King's College Hospital NHS Foundation Trust, London, UK, University of Texas MD Anderson Cancer Center, Houston, Texas, Massachusetts General Hospital, Boston, Massachusetts, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, Hôpital Saint-Antoine, Paris, France, Hôpital Saint-Louis, Paris, France, and The Christie NHS Foundation Trust, Manchester, UK.

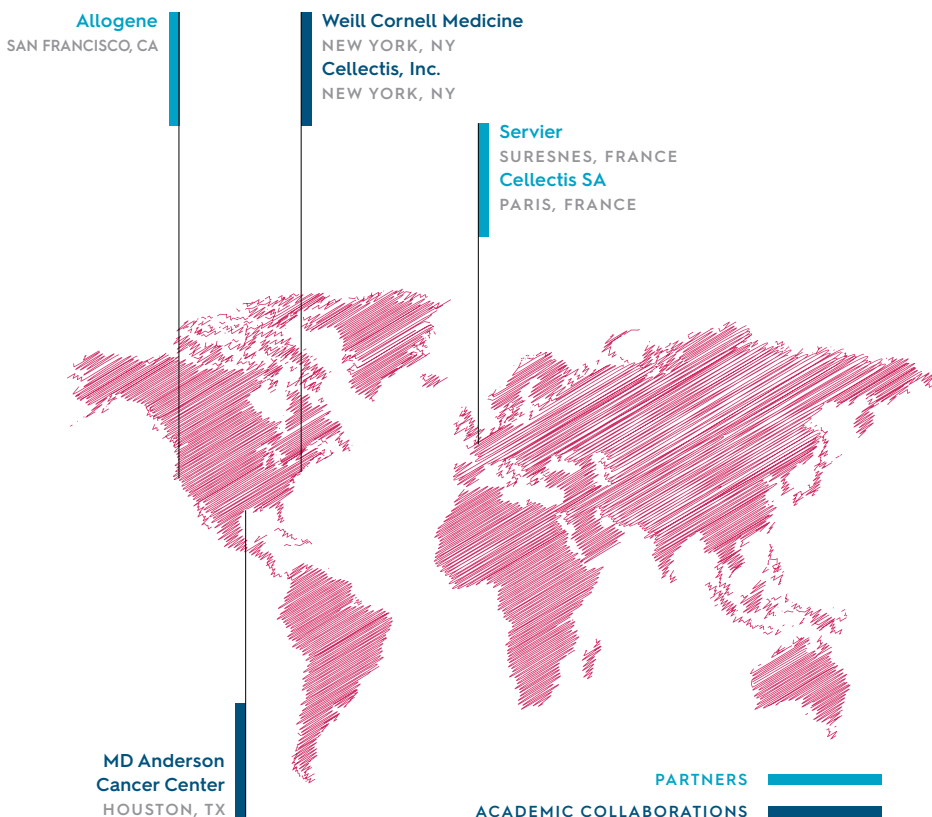
## Allogene, our new partner assuming Pfizer's role in our collaboration agreement

In June 2014, we entered into a global strategic collaboration agreement with Pfizer pursuant to which we collaborated to conduct discovery and preclinical development activities to generate CART-cells directed at targets selected by Pfizer or Collectis in the field of oncology. Pursuant to the agreement, Pfizer made an upfront, non-refundable \$80 million payment to Collectis, concurrent with Pfizer's equity investment in the Company.



In April 2018, Allogene Therapeutics, Inc. and Pfizer entered into an asset contribution agreement for Allogene to receive Pfizer's allogeneic CAR-T assets, including the Collaboration and License Agreement signed between Pfizer and Collectis in June 18, 2014.

The agreement with Allogene has the potential to provide for up to \$2.8 billion in potential clinical and commercial milestone payments to Collectis. We are also eligible to receive tiered royalties ranging in the high single-digit percentages based on annual net sales of commercialized products. Up to June 18, 2018, we may also receive funding for research and development costs associated with the Allogene-selected targets and for four Collectis-selected targets within the alliance. Allogene has exclusive rights to pursue development and commercialization of products for a total of fifteen selected targets.



## Collaborations with Weill Cornell Medicine and MD Anderson Cancer Center

In 2015, we entered into alliances with Weill Cornell Medicine and the MD Anderson Cancer Center to accelerate the development of our lead product candidates.

### **Alliance with Weill Cornell Medicine**

On June 2, 2015, Cornell University and Cellectis entered into a strategic research alliance to accelerate the development of a targeted immunotherapy for patients with AML. After conducting research and developing clinical strategies at Weill Cornell, Cellectis received in February 2017 an Investigational New Drug (IND) approval from the U.S. Food and Drug Administration (FDA) to conduct Phase 1 clinical trials with UCART123 in patients with acute myeloid leukemia (AML) and blastic plasmacytoid dendritic cell neoplasm (BPDCN).

The clinical research at Weill Cornell is led by principal investigator Dr. Gail J. Roboz, Professor of Medicine at Weill Cornell Medicine and Director of the Clinical and Translational Leukemia Programs at Weill Cornell Medicine and NewYork-Presbyterian. AML is a devastating clonal hematopoietic stem cell neoplasm that is characterized by uncontrolled proliferation and accumulation of leukemic blasts in bone marrow, peripheral blood and, occasionally,

in other tissues. These cells disrupt normal hematopoiesis and rapidly cause bone marrow failure and death. In the U.S. alone, there are an estimated 21,000 new AML cases per year, with 10,000 estimated deaths per year. In addition to the UCART123 clinical trial, Cellectis and Cornell University are working on target discovery in the AML area, in order to identify new potential targets for AML and generate new potential product candidates for AML patients.

### **Alliance with MD Anderson Cancer Center**

On September 1, 2015, Cellectis and the MD Anderson Cancer Center entered into a research and development alliance aimed at bringing novel cellular immunotherapies to patients suffering from different types of liquid tumors, particularly MM, ALL and BPDCN. Under this strategic alliance, the MD Anderson Cancer Center and Cellectis have agreed to collaboratively conduct several preclinical studies on product candidates: UCART123 for BPDCN, UCARTCS1 for multiple myeloma and UCART22 for ALL. Cellectis has agreed to provide funding and other support for these studies. The objective of the studies is to build on complementary expertise from the MD Anderson Cancer Center and Cellectis for the development of the product candidates. The MD Anderson Cancer Center and Cellectis are working together to develop and implement improvements to the research plan for the programs under joint direction of the MD Anderson Cancer Center and Cellectis' investigators. The objective of the studies is to demonstrate the functionalities and specificity of the UCART product candidates listed above, define the preclinical package required for



clinical trial applications, and prepare a clinical trial protocol and the regulatory documents required for interactions with the FDA and the clinical trial applications.

In February 2017, Cellectis received an Investigational New Drug (IND) approval from the U.S. Food and Drug Administration (FDA) to conduct Phase 1 clinical trials with UCART123 in patients with acute myeloid leukemia (AML) and blastic plasmacytoid dendritic cell neoplasm (BPDCN). The UCART123 clinical program at MD Anderson is led by Dr Naveen Pemmaraju, MD, Associate Professor, Dr Marina Konopleva, Professor, and Professor Hagop Kantarjian, MD, Department Chair, Department of Leukemia, Division of Cancer Medicine.

In May 2018, Cellectis announced the submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) requesting approval to initiate a Phase 1 clinical trial for UCART22, Cellectis' second wholly controlled TALEN® gene-edited product candidate, for the treatment of B-cell acute lymphoblastic leukemia (B-ALL) in adult patients. Pending regulatory clearance, Cellectis plans to initiate a Phase 1 clinical trial in the third quarter of 2018. The UCART22 clinical research will be led by Dr. Nitin Jain, Assistant Professor, and Prof. Hagop Kantarjian, Chairman in the Department of Leukemia and University Chair in Cancer Medicine at The University of Texas MD Anderson Cancer Center in Houston.





# Financial statements —

– Financial statements

# Tuned in with our shareholders

We finished 2017 with a plus of 72%, peaking on the Nasdaq market at \$35.01 on October 31st. The daily average volume of shares traded was 98,562 on the Euronext Growth market and 160,940 on the Nasdaq Global market.

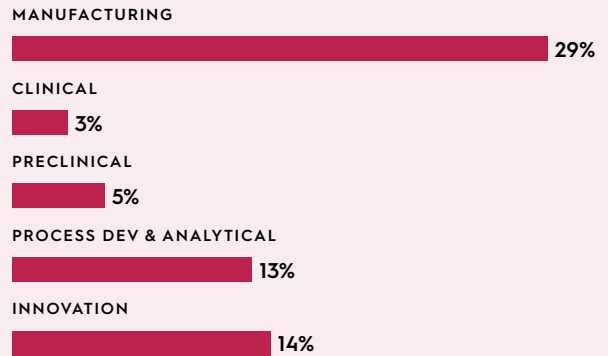
In an industry where large investments are needed to develop potentially life-saving therapies, it is important to be well financed in order to successfully achieve a series of clinical milestones. Collectis has a strong balance sheet and is well positioned to continue its progress into the years ahead.

At Collectis, we are proud of our achievements throughout 2017 and we maintained a proactive communication strategy with our shareholders. Our management team participated in more than 400 investor meetings both in the U.S. and in Europe during the year.

One General Shareholder Meeting was held on June 26, 2017, giving occasion for our management team to explain the Company's positioning in the field of immuno-oncology, elaborate on our corporate strategy and answer our shareholders' questions. In 2017, the Collectis Group issued 37 press releases, or an average of one every 10 days.

In 2017, Collectis invested \$79.2 million in Research and Development activities, which represents 62% of our total operating expenses.

## Significant R&D expenditures



## Euronext Growth



## Nasdaq



## As of December the 31<sup>st</sup>, 2017

Institutional investors France	4.3%	1,554,200
Free float other	14.3%	5,135,425
Industrial partners (incl. Pfizer)	7.9%	2,817,455
Institutional investors U.S.	24.0%	8,628,049
Investmental investors Europe & other	12.7%	4,572,866
Free float France	13.1%	4,718,004
Company related holder	23.7%	8,502,190
<b>Total</b>	<b>100%</b>	<b>35,928,189</b>

– Financial statements

# Balance sheet

## – Assets —

STATEMENTS OF CONSOLIDATED FINANCIAL POSITION – \$ in thousands

	December 31, 2016	December 31, 2017
<b>ASSETS</b>		
<b>Non-current assets</b>		
Intangible assets	1,343	1,431
Property, plant, and equipment	16,900	7,226
Other non-current financial assets	691	1,004
<b>Total non-current assets</b>	<b>18,935</b>	<b>9,661</b>
<b>Current assets</b>		
Inventories	118	250
Trade receivables	3,627	2,753
Subsidies receivables	8,723	9,524
Other current assets	8,870	13,713
Current financial assets	36,592	40,602
Cash and cash equivalents	254,568	256,380
<b>Total current assets</b>	<b>312,498</b>	<b>323,221</b>
<b>TOTAL ASSETS</b>	<b>331,432</b>	<b>332,882</b>

– Financial statements

# Balance sheet

## - Equity and Liabilities

	December 31, 2016	December 31, 2017
<b>LIABILITIES</b>		
<b>Shareholders' equity</b>		
Share capital	2,332	2,367
Premiums related to the share capital	568,185	614,037
Treasury share reserve	(416)	(297)
Currency translation adjustment	(22,174)	1,978
Retained earnings (deficit)	(207,875)	(251,927)
Net income (loss)	(67,255)	(99,368)
<b>Total shareholders' equity—Group Share</b>	<b>272,795</b>	<b>266,791</b>
Non-controlling interests	1,876	19,113
<b>Total shareholders' equity</b>	<b>274,671</b>	<b>285,904</b>
<b>Non-current liabilities</b>		
Non-current financial liabilities	30	13
Non-current provisions	560	3,430
<b>Total non-current liabilities</b>	<b>590</b>	<b>3,443</b>
<b>Current liabilities</b>		
Current financial liabilities	1,730	21
Trade payables	9,722	9,460
Deferred revenues and deferred income	38,929	26,056
Current provisions	594	1,427
Other current liabilities	5,196	6,570
<b>Total current liabilities</b>	<b>56,171</b>	<b>43,534</b>
<b>TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY</b>	<b>331,432</b>	<b>332,882</b>

## – Financial statements

# Income statement

## STATEMENTS OF CONSOLIDATED OPERATIONS

For the year ended December 31, 2017 – \$ in thousands, except per share amounts

	For the year ended December 31, 2015	For the year ended December 31, 2016	For the year ended December 31, 2017
<b>Revenues and other income</b>			
Revenues	55,864	44,808	25,188
Other income	6,701	11,637	8,528
<b>Total revenues and other income</b>	<b>62,565</b>	<b>56,444</b>	<b>33,715</b>
<b>Operating expenses</b>			
Royalty expenses	(2,746)	(1,777)	(2,620)
Research and development expenses	(58,154)	(78,458)	(79,227)
Selling, general and administrative expenses	(30,223)	(43,413)	(44,750)
Other operating income and expenses	(2,425)	(99)	232
<b>Total operating expenses</b>	<b>(93,549)</b>	<b>(123,746)</b>	<b>(126,366)</b>
<b>Operating income (loss)</b>	<b>(30,984)</b>	<b>(67,302)</b>	<b>(92,650)</b>
Financial income	10,253	7,147	7,262
Financial expenses	(1,876)	(7,101)	(18,294)
<b>Financial gain (loss)</b>	<b>8,378</b>	<b>46</b>	<b>(11,032)</b>
Income tax	–	–	–
<b>Net income (loss)</b>	<b>(22,606)</b>	<b>(67,255)</b>	<b>(103,683)</b>
Attributable to shareholders of Collectis	(22,796)	(67,255)	(99,368)
Attributable to non-controlling interests	190	–	(4,315)
<b>Basic / Diluted net income (loss) per share attributable to shareholders of Collectis</b>			
Basic net income (loss) per share (\$ /share)	(0.67)	(1.91)	(2.78)
Diluted net income (loss) per share (\$ /share)	(0.67)	(1.91)	(2.78)

– Financial statements

# Cash flow statement

## STATEMENTS OF CONSOLIDATED CASH FLOWS

For the year ended December 31, 2017 – \$ in thousands

	For the year ended December 31, 2015	For the year ended December 31, 2016	For the year ended December 31, 2017
<b>Cash flows from operating activities</b>			
Net loss for the period	(22,606)	(67,255)	(103,683)
<b>Reconciliation of net loss and of the cash provided by (used in) operating activities</b>			
Adjustments for			
Amortization and depreciation	1,937	2,211	3,371
Net loss (income) on disposals	(11)	65	40
Net financial loss (gain)	(8,378)	(46)	11,032
Expenses related to share-based payments	33,402	58,622	50,418
Provisions	(279)	(365)	2,908
Other non cash items	–	(1,432)	2
Interest (paid) / received	1,070	1,694	1,371
<b>Operating cash flows before change in working capital</b>	<b>5,135</b>	<b>(6,507)</b>	<b>(34,540)</b>
Decrease (increase) in inventories	(25)	50	(109)
Decrease (increase) in trade receivables and other current assets	1,268	(997)	(549)
Decrease (increase) in subsidies receivables	(679)	(1,122)	305
(Decrease) increase in trade payables and other current liabilities	2,961	(4,384)	(335)
(Decrease) increase in deferred income	(5,070)	(19,750)	(17,099)
<b>Change in working capital</b>	<b>(1,544)</b>	<b>(26,203)</b>	<b>(17,787)</b>
<b>Net cash flows provided by (used in) operating activities</b>	<b>3,591</b>	<b>(32,710)</b>	<b>(52,327)</b>
<b>Cash flows from investment activities</b>			
Proceeds from disposal of property, plant and equipment	111	24	7,164
Sale (Acquisition) of subsidiaries net of cash disposed of	(3,162)	–	–
Acquisition of intangible assets	(97)	(337)	(273)
Acquisition of property, plant and equipment	(4,316)	(13,696)	(2,383)
Net change in non-current financial assets	(264)	175	(125)
Sale (Acquisition) of current financial assets	–	(39,302)	(2,598)
<b>Net cash flows provided by (used in) investing activities</b>	<b>(7,728)</b>	<b>(53,137)</b>	<b>1,784</b>
<b>Cash flows from financing activities</b>			
Increase in share capital net of transaction costs	221,142	713	2,930
Shares of Calyxt issued to third parties	–	–	38,257
Decrease in borrowings	(625)	(91)	(41)
Treasury shares	75	(137)	120
<b>Net cash flows provided by financing activities</b>	<b>220,591</b>	<b>485</b>	<b>41,266</b>
<b>(Decrease) increase in cash</b>	<b>216,454</b>	<b>(85,362)</b>	<b>(9,277)</b>
<b>Cash and cash equivalents at the beginning of the year</b>	<b>136,400</b>	<b>342,111</b>	<b>254,568</b>
Effect of exchange rate changes on cash	(10,743)	(2,181)	11,089
<b>Cash and cash equivalents at the end of the period</b>	<b>342,111</b>	<b>254,568</b>	<b>256,380</b>

We present our consolidated statements of cash flows using the indirect method.

# Governance

## Executive Committee



André Choulika

### Dr. André Choulika, Chief Executive Officer

André Choulika, Ph.D., is one of the founders of Collectis and has served as Chief Executive Officer since the company's inception in 1999. He is Chairman of the Board of Directors since 2011 and President of Calyxt since August 2010. From 1997 to 1999, Dr. Choulika worked as a post-doctoral fellow in the Division of Molecular Medicine at Boston Children's Hospital, where he was one of the inventors of nuclease-based genome editing technologies and a pioneer in the analysis and use of meganucleases to modify complex genomes. After receiving his Ph.D. in molecular virology from the University of Paris VI (Pierre et Marie Curie), he completed a research fellowship in the Harvard Medical School Department of Genetics. His management training is from the HEC (Challenge +).



Julia Berretta

### Dr. Julia Berretta, VP Business Development and Strategic Planning

Julia Berretta, Ph.D., joined Collectis in 2010 in the scientific alliance and business development department. She has served as VP Business Development and Strategic Planning since 2014. Prior to joining Collectis, she worked as a researcher at the CNRS in Gif-sur-Yvette.



Elsy Boglioli

### Elsy Boglioli, Chief Operating Officer

Elsy Boglioli joined Collectis in December 2017 as Executive Vice President, Strategy and Corporate Development. Elsy has been named Chief Operating Officer in March 2018. Prior to joining Collectis, Elsy worked at the Boston Consulting Group (BCG) where she served as Partner and Managing Director, and leader of BCG's biotech-focused business in Europe. Ms. Boglioli has far-reaching expertise within the pharma and medtech industries, focusing on everything from corporate strategy and M&A to research. Ms. Boglioli graduated from Ecole Polytechnique in Paris, France and holds a master's degree in economy and management from Pompeu Fabra University in Barcelona, Spain.

### Prof. Stéphane Depil, Senior Vice President Research & Development, Chief Medical Officer

Professor Stéphane Depil, M.D., Ph.D., joined Collectis as Senior Vice President, Research & Development and Chief Medical Officer in December 2017. In addition to his role at Collectis, Stéphane Depil is an onco-hematologist at Léon Bérard Cancer Center and an adjunct Professor at University Claude Bernard Lyon 1, France. Prof.



Stéphane Depil



Depil obtained a Ph.D. in immunology at Institut de Biologie de Lille after working on a project concerning cancer vaccination. Stéphane Depil worked at Servier for 8 years in a variety of roles, including Director of Oncology Research and Development, where he managed 20 programs: 5 in the clinic, 7 at late preclinical stages, and 8 at early preclinical stages. He also directly supervised the evaluation of over 100 licensing opportunities.

#### **Dr. Philippe Duchateau, Chief Scientific Officer**

Philippe Duchateau, Ph.D., joined Collectis in 2001 to pioneer the field of gene editing and has served as Chief Scientific Officer since 2012. After receiving his Ph.D. in 1993 in biochemistry and molecular biology at the Institut Pasteur (Lille, France), he completed a research fellowship from 1993 to 2001 at the University of California, San Francisco, within the Cardiovascular Research Institute. Dr. Duchateau has led Collectis' Research department since 2004.

#### **Eric Dutang, Chief Financial Officer**

Eric Dutang, Certified Public Accountant in France, joined Collectis as Deputy Chief Financial Officer in May 2015. Eric began his career as a financial auditor with KPMG, first in Paris for five years and then in New York for two years. He worked for publicly-traded companies in France and the U.S. including Vivendi, Veolia Environnement, and Cablevision. He then became a member of the transactions and advisory teams in Paris for seven years where he carried out acquisitions/disposals for both publicly-traded companies and private equity funds. Eric holds a Master of Finance and Executive MBA from HEC Paris (France)/ Babson Massachusetts (USA).

#### **Stephan Reynier, Chief Regulatory and Compliance Officer**

Stephan Reynier, M.Sc., joined Collectis in April 2011. He serves as Chief Regulatory and Compliance Officer since 2014 with the responsibilities of ensuring a speedy and successful development of the UCART product family by establishing close interactions with regulatory agencies such as the EMA and the FDA, while securing compliance to applicable regulations, regulatory guidelines and quality assurance standards. From his previous positions as senior Director at Voisin Consulting Life Sciences and European Associate Director of Medical Affairs at Gilead sciences, Mr. Reynier has extensive experience in the design and implementation of regulatory strategies for the development of drugs and biologics, with a strong focus on cell and gene therapy. Mr. Reynier graduated as Agro-Engineer in France and received a Master of Science in Chemical Engineering from the University of Toronto, Canada.

#### **Dr. David Sourdive, Executive Vice President Technical Operations**

David Sourdive, Ph.D., is a co-founder of Collectis and joined the Board of Directors in 2000. Dr. Sourdive holds the position of Executive Vice President, Technical Operations, with the mission to develop the Company's industrial and technological basis as well as to deploy its operations in the pharmaceutical arena. Dr. Sourdive combines a strong scientific expertise with experience in managing industrial programs, bringing innovative technologies to industrial fruition. He served as Executive Vice President, Corporate Development, from 2008 to 2016. In addition to his role at Collectis, David Sourdive graduated from École Polytechnique, received



Philippe Duchateau



Eric Dutang



Stephan Reynier



David Sourdive

his Ph.D. in molecular virology at Institut Pasteur, and completed a research fellowship in the Emory University Department of Microbiology and Immunology. His management training is from the HEC (Challenge +) and his decade-long experience in industrial program management was acquired at the French Department of Defense (DGA) prior to Collectis' inception.

#### **Marie-Bleuenn Terrier, General Counsel**

Marie-Bleuenn Terrier joined Collectis as Legal Counsel in 2008, and was appointed General Counsel in 2013. Prior to joining Collectis, she worked as Legal Counsel for Pfizer from 2004 to 2006, and for Boehringer Ingelheim from 2006 to 2008. Marie-Bleuenn Terrier has served as secretary of the Board of Directors of Collectis since 2015. She holds a Master's degree in Law from the Panthéon La Sorbonne University in Paris.



Marie-Bleuenn Terrier



Federico A. Tripodi

#### **Federico A. Tripodi, Chief Executive Officer of Calyxt, a subsidiary of Collectis**

Federico A. Tripodi was appointed CEO of Calyxt in May 2016. He holds a Master of Business Administration degree from Washington University's Olin Business School, as well as an agronomic engineering degree from Buenos Aires University, and has gathered extensive experience in agricultural R&D and product development during his nearly two-decade career in the ag biotech and seeds industry. Prior to joining Calyxt, Mr. Tripodi worked as General Manager for Monsanto Company's sugarcane division in Brazil for three years. He held other roles for Monsanto in St. Louis, MO, spanning Corporate Strategy, Omega-3 Program Lead, Oilseeds Global Quality Management Lead and multiple other roles that involved managing multidisciplinary research teams.

## Board of Directors

#### **Dr. André Choulika, Ph.D.**

Chairman of the Board of Directors and CEO

#### **Laurent Arthaud**

Independent Director\*

#### **Pierre Bastid**

Independent Director\*

#### **Dr. Rainer Boehm, MD**

Independent Director\*

#### **Alain Godard**

Independent Director\*

#### **Hervé Hoppenot**

Independent Director\*

#### **Jean-Marie Messier**

Independent Director\*

#### **Dr. Annick Schwebig, MD**

Independent Director\*

#### **Dr. David Sourdive, Ph.D.**

Director and Executive Vice President  
Technical Operations

*\*Independent Director according to Nasdaq and SEC rules*

# Committees of the Board of directors

## Audit and Finance committee

Pierre Bastid, Independent Director\*

Laurent Arthaud, Independent Director\*

Jean-Marie Messier, Independent Director\*

## Compensation Committee

Alain Godard, Independent Director\*

Dr Annick Schwebig, Independent Director\*

# Clinical Advisory Board

**Prof. Catherine Bollard**, Chief, Division of Allergy and Immunology at the Children's Research Institute, Children's National Health System and The George Washington University, Washington, DC

**Prof. Hervé Dombret**, Head of the Leukemia Unit at the Hôpital Saint Louis, Paris, and Director of Clinical Research in the Hematology, Immunology and Transplantation Unit, University of Paris Diderot, Paris, France

**Prof. John Gribben**, Lead of the Centre for Hemato-Oncology, Barts Cancer Institute of London, UK

**Prof. Ola Landgren**, Chief of Myeloma Service at Memorial Sloan Kettering Cancer Center, New York, NY

**Dr. Marcela Maus**, Director of Cellular Immunotherapy at the Massachusetts General Hospital, Boston, MA

**Prof. Dietger Niederwieser**, Professor of Medicine, Head of the Division of Hematology and Medical Oncology at the University of Leipzig, Germany

**Prof. Kanti Rai**, Professor of Medicine and Molecular Medicine, Hofstra Northwell School of Medicine, Hempstead, NY

**Prof. Catherine Thieblemont**, Professor of Hematology in the Paris VII- University, France and Head of the Hemato-Oncology Unit of St-Louis Hospital, Paris, France

**Prof. Koen van Besien**, Director of the Stem Cell Transplant Program and Professor of Medicine at Weill Cornell Medical College, New York, NY

# External Auditors

## Statutory Auditor

Ernst & Young

JMH Conseils

# Calyxt —



— Calyxt

# Calyxt in brief



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**Prof. Daniel Voytas,**  
Chief Scientific Officer  
of Calyxt, inc.

Calyxt is a consumer-centric, food- and agriculture-focused company. By combining its leading gene-editing technology and technical expertise with its innovative commercial strategy, Calyxt is pioneering a paradigm shift to deliver healthier food ingredients, such as healthier oils and high fiber wheat, for consumers. While the traits that enable these characteristics may occur naturally and randomly through evolution—or under a controlled environment through traditional agricultural technologies—those processes are imprecise and take many years, if not decades. With its technology, Calyxt is able to precisely and specifically edit a plant genome to elicit the desired traits and characteristics, resulting in a final product that has no foreign DNA. Calyxt believes the precision, specificity, cost effectiveness and development speed of its gene-editing technologies will enable them to provide meaningful disruption to the food and agriculture industries.

Food-related issues, including obesity and diabetes, are some of the most prevalent health issues today and continue to grow rapidly. As awareness of these diet-related health issues grows, consumers are emphasizing a healthier lifestyle and a desire for nutritionally rich foods that are more nutritious, better tasting, less processed and more convenient. This trend is leading to an increase in the demand for higher valued, premium segments of the food industry, such as higher fiber, reduced gluten and reduced fat products. As a result of these trends, food companies are looking for specialty ingredients and solutions that can help them satisfy their customers' evolving needs and drive growth in market share and new value-added products.

While food companies are focused on these trends, Calyxt believes the legacy agriculture companies have overlooked society's food-related issues and are not properly equipped to address health-driven consumer food trends. These legacy agriculture companies have historically focused on increasing yields and volume—to address population growth—while increasing profit margins and market share by reducing input costs. They have been burdened by high research and development costs and a high degree of commoditization in their deep, farmer-focused supply chains.

Its proprietary gene-editing technologies and innovative commercial strategy allow Calyxt to bridge the divide between evolving consumer preferences and the historical approach by the large legacy companies in the agriculture supply chain. Calyxt edits the genome of food crops by using "molecular scissors" to precisely cut DNA in a single plant cell, uses the plant's natural repair machinery to make the desired edit and finally regenerate the single cell into a full plant. Calyxt is able to develop targeted traits—some of which

would be nearly impossible to develop using traditional trait-development methods—quicker, more efficiently and more cost effectively than traditional trait-development methods. With its technology, Calyxt is well-positioned to assess the probability of success early on in the research and development process, potentially eliminating expensive late stage failures and allowing for a larger breadth of products to be developed. Calyxt has a strong track record as it has successfully edited more than 20 unique genes in 6 plant species since our inception in 2010.

Calyxt's commercial strategy is centered on developing healthier specialty food ingredients to enable the food industry to address evolving consumer needs. This involves developing and leveraging its supply chain to effectively bring its consumer-centric products to the marketplace. Calyxt intends to repurpose and leverage existing supply chain capacity by contracting, tolling or partnering with players in the existing supply chain, such as seed production companies, farmers, crushers, refiners or millers, which will allow Calyxt to apply its resources to maximizing innovation and product development while minimizing its capital expenditures and overhead.



# Highlights

## **New Technology Framework Agreement with Plant Bioscience Limited to Expand IP Portfolio**

March 9, 2017

## **Appointment of Cargill Executive Manoj Sahoo as Chief Commercial Officer**

March 21, 2017

## **Calyxt Patent Encompassing Broad Uses of Plant Gene Editing Technologies Maintained by USPTO**

May 10, 2017

## **Launch of U.S. Field Trials with University of Minnesota for Powdery Mildew-Resistant Spring Wheat Variety**

May 16, 2017

## **Full Exercise of Over-Allotment Option and Closing of Calyxt Initial Public Offering**

July 25, 2017

## **Calyxt Broke Ground on New Concept-to-Fork Facility in Roseville, Minn.**

September 6, 2017

## **Improved Oil Composition Canola Product Candidate Advanced to Phase I**

September 25, 2017

## **Calyxt and S&W's Gene-Edited Alfalfa Plant Designated as Non-Regulated by USDA**

October 2, 2017

## **Calyxt and Farmer's Business Network, Inc. Partner to Expand Grower Base for Calyxt's Identity-Preserved High Oleic Soybeans**

December 12, 2017

- Calyxt

# Product overview



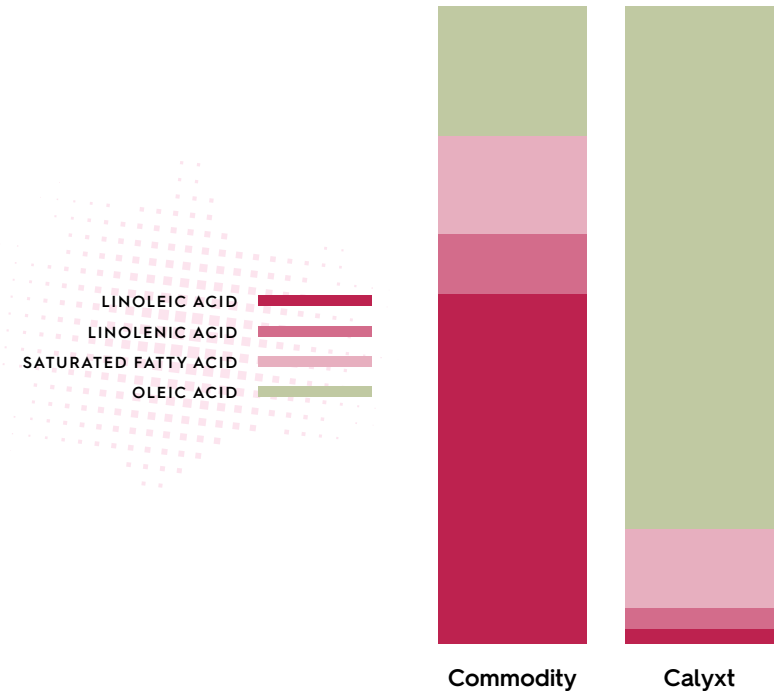
19 Products under development across 5 crops : soybean, wheat, alfalfa, canola and potatoe

## High oleic soybean —a premium oil market commercial opportunity

Soybean oil has historically been partially hydrogenated to enhance its oxidative stability in order to increase shelf life and improve frying characteristics. This process, however, creates trans-unsaturated fatty acids, or trans fats, which have been demonstrated to raise low-density lipoprotein (LDL) cholesterol levels and lower high-density lipoprotein (HDL), both of which contribute to cardiovascular disease. This discovery led the FDA to rule in 2003 that manufacturers be required to include trans fat content information on the “Nutrition Facts” label of foods. In 2015, the FDA took a further step and banned the use of partially hydrogenated oils, the primary dietary source of artificial trans fat in processed foods, by all food manufacturers beginning in 2018.

Monounsaturated fats, such as oleic acid, have been linked to reducing LDL cholesterol and triglycerides and raising HDL cholesterol. Diets rich in monounsaturated acids are associated with lower fat mass and decreased blood pressure.

Calyxt developed a soybean trait that has produced oils with a fatty acid profile that



contains 80% oleic acid, 20% less saturated fatty acids compared to commodity soybean oil and zero trans fats, as shown in the chart above.

Calyxt’s high oleic soybean oil offers additional potential benefits, including reduced saturated fats, a threefold increase in fry-life, and reduced polymerization upon frying at high temperatures. Soybean oil is also neutral in flavor, odorless and colorless, and is therefore highly desired as a food ingredient because it has limited impact on the sensory characteristics of the final food product.



Calyxt's soybean product candidate is in Phase 3 of its development process, and Calyxt is currently completing its commercialization plan and anticipate commercialization by the end of 2018.

## High fiber wheat

Fiber is the indigestible portion of food that is essential for healthy digestion. Research has shown that fiber may play a large role in maintaining bowel health, lowering cholesterol, stabilizing blood glucose levels and controlling weight gain. A high fiber diet has the potential to lower the rate of glucose entry into circulation, thus decreasing the risk of food-related chronic diseases, such as coronary artery disease and diabetes. The average American adult consumes approximately 15-18 grams of fiber daily, only half of the amount recommended by the U.S. Department of Health's dietary guidelines based on the average caloric intake. In recent years, the awareness of the health benefits of high fiber diets has increased. This has translated to a strong growth in demand for high fiber food products, with 38% of grocery shoppers now seeking high fiber foods. Calyxt is developing high fiber wheat traits that could be used to produce white flour with up to three times more dietary fiber than standard white flour. Calyxt anticipates that by altering the proportion of certain slower digested carbohydrates in the wheat grain, it will increase dietary fiber. This would allow consumers to reach their daily value of fiber without changing their existing food preferences. These high fiber wheat product candidates will not contain any foreign DNA.



Calyxt believes its high fiber wheat flour will be incorporated into many food products—from pasta to bread. Whereas a single serving of whole wheat flour can provide 49% of an individual's daily fiber needs, a single serving of Calyxt's high fiber flour may provide up to 100% of the recommended daily requirement thereby allowing food manufacturers to make high fiber products sought after by many consumers.

This product candidate is currently in Phase 1 of its development process and may launch as early as 2020 - 2021.

White Wheat Flour		
<b>Nutrition Facts</b>		
Serving Size 100g		
<b>Total Carbohydrate</b>	<b>73 g</b>	<b>24%</b>
<b>Dietary Fiber</b>	<b>12 g</b>	<b>48%</b>
<b>Sugars</b>	<b>0 g</b>	

White Wheat Calyxt Flour		
<b>Nutrition Facts</b>		
Serving Size 100g		
<b>Total Carbohydrate</b>	<b>73 g</b>	<b>24%</b>
<b>Dietary Fiber</b>	<b>25 g</b>	<b>100%</b>
<b>Sugars</b>	<b>0 g</b>	

A single serving of Calyxt high fiber flour may provide up to 100% of the recommended daily value.

— Calyxt

# Management team

## **Dr. André Choulika, Chairman of the Board**

## **Federico Tripodi, Chief Executive Officer**

## **Dr. Dan Voytas, Chief Science Officer**

Dan graduated *summa cum laude* from Harvard College in 1984 and received his Ph.D. in genetics from Harvard Medical School in 1990. He is a co-founder of Calyxt and one of the inventors of the TALEN® technology. He continues to optimize the use of TALEN® for the targeted modification of plant genomes. In addition to his role at Calyxt, Dr. Voytas is a professor in the Department of Genetics, Cell Biology and Development at the University of Minnesota (UMN), which he joined in 2008, and Director of UMN's Center for Genome Engineering. In 1992, Dr. Voytas joined the faculty at Iowa State University. Prior to this, he conducted postdoctoral research at Johns Hopkins University School of Medicine. Dan is an elected Fellow of the American Association for the Advancement of Science.

## **Michel Arbadji, Director of Business Development**

Michel joined Calyxt in July 2015 as Director of Business Development, and manages the external supply chain operations. Michel received his Agriculture Engineering degree and Master in Economics and Agriculture Machinery from the Institut National Agronomique Paris Grignon in Paris, France. Prior to joining Calyxt, Michel headed the European and Middle East Operation for Signature Control Systems, where

he built and managed the distribution network, EU marketing, and sales. Michel started his career at the Toro Company EMEA, where he held several positions in business development, sales, and marketing. Over his 27-year career, he has successfully built several pioneering businesses from the R&D stage to setting up large-scale distribution channels.

## **Bryan W. J. Corkal, Chief Financial Officer**

Bryan joined Calyxt in December 2016 as Chief Financial Officer, and manages the company's day-to-day financial operations. Bryan received his MBA from York University in Toronto, Canada and a B.Sc. in Civil Engineering from the University of Manitoba. Bryan is a CFA charter holder and is a CPA in the state of Missouri. Bryan brings extensive finance and commercial experience in the seeds and traits agricultural sector, having worked over 17 years at Monsanto in a variety of finance and strategy roles, including the acquisition and integration of several companies. Early in his career, Bryan worked for Ernst & Young and Delcan Corporation as a consultant on a number of projects throughout Canada and Latin America.

## **Glenn Bowers, Vice President of Breeding**

Glenn Bowers is Vice President of Breeding with responsibilities for breeding, field trialing and seed production for all crops. Glenn has a M.S. and Ph.D. in Plant Pathology with a focus on breeding and the genetics of resistance. He spent 17 years managing a soybean breeding

program with Texas A&M University, followed by a year doing the same at Purdue University. He then spent 16 years with Syngenta, first managing a soybean breeding program and then as global head of soybean breeding. Glenn is a certified project manager (PMP), and his background lends him extensive experience in delivering products, both globally and stateside, through effective collaboration between marketing and supply chain. He is skilled in creating, developing, and managing diverse and globally dispersed teams, and he possesses a deep knowledge of and experience in field trialing, disease phenotyping, and agronomy.

#### **Manoj Sahoo, Chief Commercial Officer**

Manoj Sahoo holds a MBA from the Tuck School of Business at Dartmouth and a Bachelor's degree in Chemical Engineering from the National Institute of Technology in India. Manoj has more than two decades of experience working in a variety of roles covering commercial, strategy, business development and M&A for global corporations in the ag, food, energy and materials fields. Prior to joining Calyxt, Manoj was Assistant Vice President for Food Ingredients and Bio-industrial Enterprise at Cargill. Over the years, Manoj has also served on the boards of both Calysta Inc. and Rivertop Renewables as a Cargill representative. He also serves on the Industry Advisory Board of Larta Institute which assists the USDA, NIH and NSF with the commercialization assistance program.

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